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FAILURES AFTER IMMUNIZATION WITH *HAEMOPHILUS INFLUENZAE* TYPE b VACCINES — 1991-1995

Since January 1991, the 10 pediatric centres that participate in the Immunization Monitoring Program, Active (IMPACT) have conducted surveillance for admissions resulting from infection with *Haemophilus influenzae* type b (Hib). The structure of this surveil- lance network, which is jointly sponsored by the Laboratory Centre for Disease Control (LCDC) and the Canadian Paediatric Society (CPS), has been described previously[1]. In brief, the nurse monitors, who search out cases at each centre, are able to use multiple ascertainment methods (laboratory records, medical records, ward searches) and to abstract detailed information about each case, including the immunization history. Monitors can elicit immunization details from additional sources when necessary. As a result, a number of Hib vaccination failures have been recognized, the details of which are presented in this report.

Methods

The surveillance period covered by this report extended from 1 January, 1991 to 30 June, 1995. Surveillance was entirely prospective at five centres and both retrospective and prospective at five centres that joined the network in 1993. All centres used both microbiology laboratory results and hospital discharge codes to identify cases throughout the surveillance period. Search methods (including ICD9 discharge codes) and case definitions were standardized. Case information and vaccination details were reported on a custom- designed form. Reports were scrutinized for completeness at a data coordinating centre prior to being entered into a database.

The case definition for vaccination failure was the onset of culture-confirmed, invasive (i.e., involving a normally sterile body fluid) Hib infection more than 28 days following completion of age-appropriate immunization for the specific Hib vaccine used.

Results

During the surveillance period, a total of 351 Hib cases were identified at participating centres. Fifty-seven of these 351 children had previously received one or more doses of Hib vaccine. Of these 57 cases, 40 met the case definition for vaccination failure and are described here. Twenty-four of these children were boys and 15 were girls. Gender was not specified in one instance. The median age was 3 years, the mean 40.8 months. Seven cases occurred in children 6 to 8 years old, when Hib cases are generally infrequent. Only eight cases (20%) had underlying medical problems that might have predisposed to Hib infection, including four with heart or lung problems (two of these children had Down syndrome), one with an immunologic defect (congenital lymphangiectasia), and three with immunosuppression (one following kidney transplantation, two with severe burn injuries).

The presenting syndromes included epiglottitis (18 cases), meningitis (11), pneumonia with bacteremia (6), fever with bacteremia (4), and osteomyelitis (1). Epiglottitis was present in six of 18 (33%) children 0 to 2 years of age and in 12 of 22 cases (54%) 3 to 8 years of age, a difference that is not statistically significant. Other syndromes also did not differ significantly in frequency by age.

The interval between completion of Hib vaccination and the onset of Hib infection ranged from 4 months to 82 months, with a mean interval of 27.8 months. The number of cases in previously vaccinated children was relatively constant at 8 to 12 cases per year. In 1994, when 24 cases of Hib disease were reported, nine vaccination failures represented 38% of the total.

The attribution of vaccination failures is summarized in Table 1. The largest number followed administration of PRP-D (ProHIBiT™) vaccine, which was recorded by name in 18 instances and was the only vaccine supplied at the time in 11 other instances (where only "Hib vaccine" was recorded in providers' records), for a total of 29 failures. Failures that occurred prior to 1991, after a relatively short interval following vaccination, would not have been captured by our surveillance.

Table 1
Summary of *Haemophilus Influenzae* Type b Vaccines Given to Children Who Later Developed Hib Infection

Product	Cases	Period of Use
PRP polysaccharide		1986-88
by product name	1	
by inference*	3	
PRP-D (ProHIBiT™)		1988-92
by product name	18	
by inference*	11	
PRP-T (Act-HIB®)	3	1992-
HbOC (HibTITER®)	3	1992-
Unattributable (1993 cases)	1	
TOTAL	40	

* Based upon product supplied by province at the time of vaccination and age at vaccination.

Vaccination failures following use of named, contemporary vaccines numbered only six. None followed PRP-OMP (PedvaxHIB®) vaccine, which had limited use in Canada. Three cases each were seen after use of PRP-T (ActHIB®) and HbOC (HibTITER®), respectively. In those three children receiving the PRP-T, the vaccine was administered in a mixture with DPT or DPT-IPV vaccine, as recommended by the manufacturer.

The failures after PRP-T were as follows:

1. A 16-month-old girl with severe burns to her skin who developed Hib pneumonia and bacteremia despite vaccination at 3, 6 and 8 months of age. She recovered from the infection but died of her wounds.
2. A 31-month-old boy with severe burns to his skin who developed Hib pneumonia and bacteremia despite vaccination at 16 months of age. This child survived.
3. A 15-month-old, previously healthy boy who developed Hib epiglottitis 9 months after completing Hib vaccination. Primary doses were given at 2, 4 and 6 months of age. This child recovered.

The failures after HbOC vaccine were as follows:

1. A 15-month-old boy who developed Hib epiglottitis 10 months after completing vaccination (doses at 1, 3 and 5 months). The child was previously healthy. He recovered.
2. A 15-month-old boy who developed Hib meningitis despite vaccination at 2, 4 and 6 months of age. He was previously healthy. Immunologic investigations revealed hyporesponsiveness to PRP polysaccharide. This case was reported previously[2].
3. A 3½-year-old boy who developed Hib epiglottitis despite vaccination at 19 months of age. He was previously healthy and recovered fully.

Discussion

While recognition of failures is a desirable component of the evaluation of any vaccination program, it is not always achievable through routine reporting mechanisms. This is particularly true of Hib cases, as laboratory-based reports or voluntary case reports often lack details of prior immunizations. The nurse monitors in the IMPACT system are ideally positioned to search out this information for Hib cases at the 10 (now 11) participating hospitals. The IMPACT group reported the first recognized failure of a contemporary Hib vaccine in Canada[2]. This report describes the first extensive series of Hib vaccination failures in Canada, although others have reported case series from the United States[3]. Our attribution of failures was confounded by providers' inattention to recording Hib vaccine names, particularly earlier when only single products were widely used for extended periods. The same situation made it possible for us to infer the product name in most instances.

The 40 vaccination failures included in this report accounted for 11.4% of Hib cases seen at IMPACT centres during the surveillance period. As the total number of cases declined from year to year[4], the number of vaccination failures remained relatively constant at 8 to 12 per year. Consequently, the proportion of cases resulting from vaccination failure increased from 4.9% (8 of 163) in 1991 to 38% (9 of 24) in 1994.

The great majority of affected children were considered normal and healthy prior to the onset of Hib infection. Given that the mean age of cases was 40.8 months, most instances of severe immunodeficiency would have been recognized before this time. However, few of our cases were investigated for subtle immunologic problems, such as specific hyporesponsiveness to Hib PRP polysaccharide (documented in one case)[2] or IgG subtype disorders[3].

Most vaccination failures (83%) followed the two earliest vaccines, PRP polysaccharide (four cases) and PRP-D conjugate (29 cases). The former was in limited use for only 2 years but the latter was widely used for 4 years, with all provinces but one having routine programs. In studies conducted following its licensure in the U.S., PRP-D vaccine efficacy was estimated at only 74% to 88%[5,6]. Thus, it is not surprising to encounter some vaccination failures; we will likely continue to do so for a number of years. Reduced circulation of Hib as a result of widespread vaccination may help to protect inadequately immunized children[7] but our seven cases in older children indicate that herd immunity is an imperfect means of protection.

Vaccination failures after the two contemporary Hib vaccines were few but follow-up extends only from 1992, when all provinces implemented infant-based programs. Between 1992 and 1994 manufacturers reported Canadian distribution totals of 7,324,305 doses of HbOC vaccine and 2,750,841 doses of PRP-T vaccine (P. Duclos, Bureau of Infectious Diseases, LCDC; personal communication, 1995). With all provinces now using PRP-T vaccine, it is noteworthy that only three failures have been detected after its administration. Two involved children with severe burns, a situation known to predispose to invasive infections through loss of immunoglobulins and complement components. The third case involved an apparently normal child infected at 15 month of age. Studies of vaccinated infants[8] have shown a substantial decline in serum anti-PRP levels prior to booster dose administration at 18 months, a phenomenon that might predispose those with low antibody levels to infection. No failures have been detected following administration of the booster (fourth) dose of PRP-T, but follow-up of such children is limited. Active,

population-based surveillance for Hib cases is in progress in several provinces that use PRP-T vaccine.

As Hib cases decline in number, physicians should take particular note of cases that represent vaccination failure. Such cases should be reported to public health authorities and to the vaccine manufacturer. Cases after administration of contemporary vaccines like PRP-T should be considered for immunologic investigations, particularly for defects in immunoglobulin synthesis, including IgG subtypes[3].

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Source: *D Scheifele, MD, R Gold, MD, V Marchessault, MD, P Duclos, DVM, PhD, and Members of the LCDC/CPS IMPACT Group.*

RESPIRATORY VIRUS SURVEILLANCE, WINTER 1995-1996 — CANADA

The accompanying figures show the numbers of specimens submitted for testing and the numbers of laboratory-confirmed cases of influenza, parainfluenza, respiratory syncytial and adeno viruses recorded to date (27 August, 1995 — 6 January, 1996) for this winter season.

Influenza

To date, 447 reports of influenza virus have been received: 445 influenza A (all 159 strains subtyped were H1N1) and two influenza B viruses. Reporting began to increase in mid-November, mainly in the Prairies, with fewer numbers reported from British Columbia and Quebec. Activity appears to have peaked at the turn of the year.

Parainfluenza

A total of 232 reports of parainfluenza virus infection have been recorded (type 1, 153; type 2, 53; and type 3, 26), most coming from the Prairies and Ontario. Early cases were recorded in September and there has been no obvious peak in reporting to date.

Respiratory Syncytial Virus

This season, 500 reports of RSV infection have been recorded: 191 (38%) from Quebec, 95 (19%) from Ontario, 191 (38%) from the Prairies, and 23 (5%) from British Columbia. The numbers of cases reported have continued to increase since mid-November.

Adenovirus

A relatively low number of adenovirus cases (148) have been recorded, most coming from Quebec (33) and the Prairies (101).

Source: *Laboratories contributing to the Respiratory Virus Surveillance Program, Division of Disease Surveillance, Bureau of Infectious Diseases, LCDC, Ottawa.*

See charts on the next page

Notifiable Diseases Summary

We have excluded this table from the FAX issue of Canada Communicable Disease Report for those readers who do not need this information. For those readers interested in this table, call the FAX line and select the index to get the access number.

Notifiable Diseases Summaries published to date in this new format (FAX) can be found in the index under the same name.

Figure 1.
Positive Influenza Tests in Canada, by Region, by Week of Report

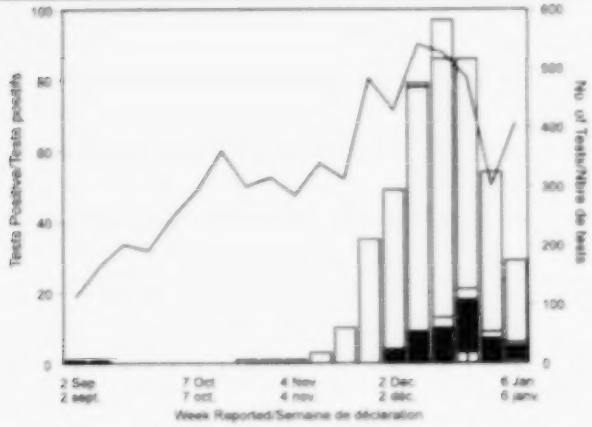

Tests Positive/Tests positifs
No. of Tests/Nbre de tests
2 Sep / 2 sept.
7 Oct / 7 oct.
4 Nov / 4 nov.
2 Dec / 2 déc.
6 Jan / 6 janv.
Week Reported/Semaine de déclaration

Figure 3.
Positive RSV Tests in Canada, by Region, by Week of Report

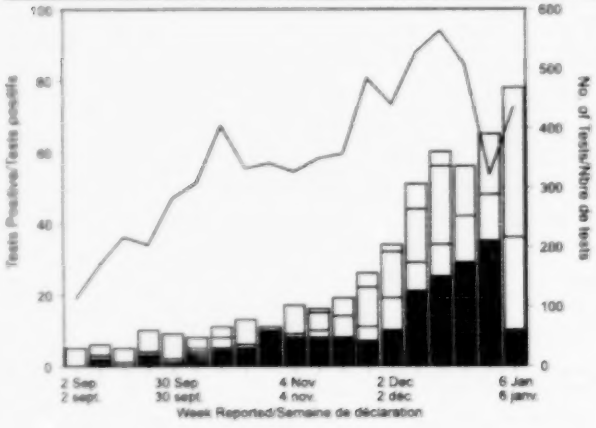

Tests Positive/Tests positifs
No. of Tests/Nbre de tests
2 Sep / 2 sept.
30 Sep / 30 sept.
4 Nov / 4 nov.
2 Dec / 2 déc.
6 Jan / 6 janv.
Week Reported/Semaine de déclaration

Figure 2
Positive Parainfluenza Tests in Canada, by Region, by Week of Report

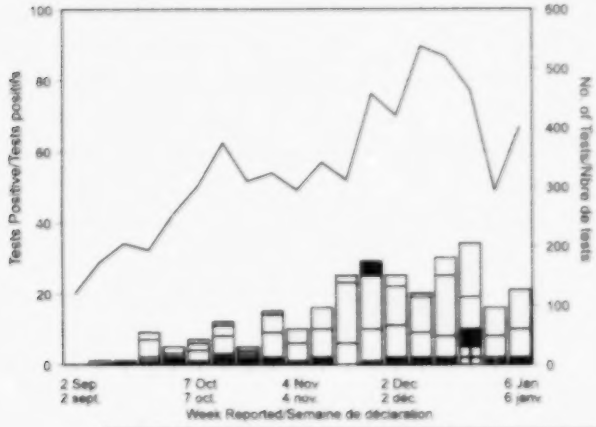
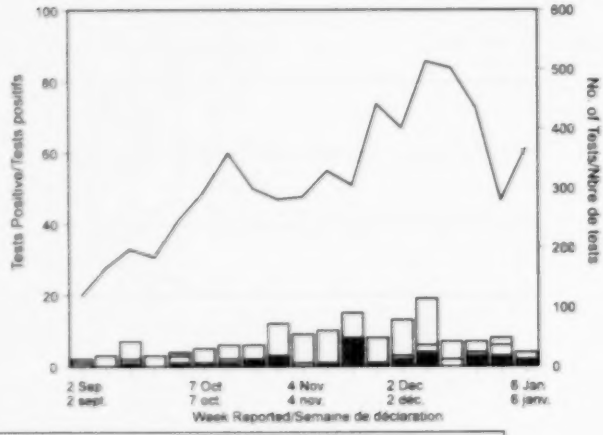
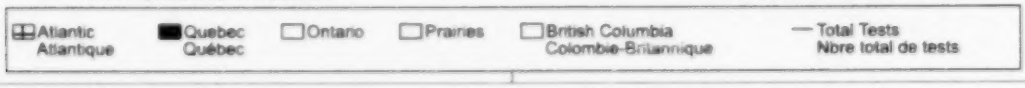

Tests Positive/Tests positifs
No. of Tests/Nbre de tests
2 Sep / 2 sept.
7 Oct / 7 oct.
4 Nov / 4 nov.
2 Dec / 2 déc.
6 Jan / 6 janv.
Week Reported/Semaine de déclaration

Figure 4.
Positive Adenovirus Tests in Canada, by Region, by Week of Report


Tests Positive/Tests positifs
No. of Tests/Nbre de tests
2 Sep / 2 sept.
7 Oct / 7 oct.
4 Nov / 4 nov.
2 Dec / 2 déc.
6 Jan / 6 janv.
Week Reported/Semaine de déclaration



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